

Vitamin C and the Menstrual Function

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With a statistical analysis and commentary by R. C. Geary, D.SC.

FOR some years it has been known that the anæmia from which large numbers of women of the industrial classes suffer, is due to the frequent losses of blood in pregnancy or from menorrhagia. This was demonstrated first by Davidson, Fullerton,¹ Orr,² and others, in two surveys, carried out in Aberdeen in 1933 and 1935. In the first survey, it was shewn that there was extensive anæmia amongst women in a section of the industrial population of the city. Men and children did not suffer to the same degree. A dietary investigation revealed that a normal blood picture could be maintained on a diet containing much less iron than the amount generally regarded as necessary (fifteen mg. per diem). There was no correlation between the anæmia and the content of iron in the diet, but a definite correlation was found to exist between anæmia, pregnancy, and menorrhagia. In the group of women who exhibited anæmia, an overwhelming number had either one or other of these disabilities. It was considered that since some function of womanhood was responsible for the anæmia, and that blood-loss either from menorrhagia or pregnancy was the deciding factor, then diets capable of maintaining men or children were not sufficiently rich to compensate for the heavier requirements of women. It was not possible to estimate the vitamin content of the diets. In the later survey in 1935, hæmoglobin estimations were carried out on three thousand people. Analysed in groups, it was found that anæmia was most prevalent during the first year of life and during the period of child-bearing. Sixteen per cent. of adolescent and forty-five per cent. of adult women were regarded as anæmic. Anæmia was absent in adolescent and adult males except in association with disease. The more severe cases were treated with iron, and the hæmoglobin content rapidly restored to normal.

Vitamin C also plays a part in regulating the level of hæmoglobin in the blood, and it might be postulated that those who exist on a diet deficient in iron are also likely to be deficient in vitamin C. Deficiency in vitamin C will produce anæmia—such as is seen in scurvy—even on a diet containing sufficient iron. It has been possible to cure persons suffering from anæmia, by a diet containing little iron, but plenty of vitamin C. Leverton and Roberts³ carried out daily hæmoglobin estimations and red blood cell counts on four women: two for three months and two for four. Complete analysis of diet, excreta, and menstruum was also undertaken during this time. They found that there was no relation between the menstrual flow and the variations which were noted in the Hb. They observed daily variations in the Hb. content as follows:—fifty-seven per cent. were no greater than 0.5 gm. and eighty per cent. were no greater than one gm. In the majority of cases it was not greater than experimental error. The average standard deviation for Hb. was 0.9 gm. The four subjects showed a rise in Hb. content over the period of study. This was a slow upward trend and was not accompanied by any rise in the red cell count. The increases amount in each case to one gm. or more

of hæmoglobin per hundred c.c. of blood. It was accentuated in the case of one of the subjects who received an additional dose of iron in the fourth and fifth cycles. But the rise was also seen in the other three who had not had this supplement, but who were maintained on a very complete diet with a daily iron content of ten to fifteen mgm. On the diet—at that time considered to fulfil normal requirements—the subjects were able to store a measurable quantity of iron.

Apart from its influence on the level of Hb., vitamin C may help to cause “nutritional anæmia” in other ways. Vogt⁴ used vitamin C with success in the treatment of “juvenile hæmorrhages.” He ascribes its action to a strengthening of the walls of vessels, and found it of especial value in cases of essential thrombopenia. Junghaus⁵ treated thirty-five women who suffered from climacteric, pre-climacteric menorrhagia, and other forms of gynæcological hæmorrhages. The treatment was successful in thirty-three cases. Siegert⁶ emphasises the clinical significance of Gaethgen’s observation, that vitamin C deficiency is common in pregnancy. According to his findings, the vitamin C metabolism of women during pregnancy is always on the border-line of hypovitaminosis. This is most marked in winter, when the diet is poor in the vitamin. In women who were deficient in vitamin C and who suffered from uterine hæmorrhage of unknown origin while pregnant, he was able to obtain prompt healing by giving vitamin C.

Müller⁷ achieved good results in the treatment with vitamin C of gynæcological and other hæmorrhages, when these were caused by a C hypovitaminosis. The improvement in the symptoms went parallel with the increase of the reducing property of the urine. If it was found that the greater part of the vitamin C was excreted from the first day onwards, then it showed that the system was supplied with enough vitamin C, so that no retention was necessary. In these the vitamin C therapy was unsuccessful. In the cases treated, the amount of the deficit was ascertained by the usual functional tests, and the dosage regulated accordingly. The results were good in the cases of juvenile, pre-climacteric, and climacteric metrorrhagia, and in cases of hæmorrhage from the myomatous uterus. Gastric hæmorrhage, and one case of bleeding from the nose and lungs, were also influenced. C hypovitaminosis was also shown to be present in a case of aphthous stomatitis, and was cured by vitamin C therapy.

Huckel⁸ used vitamin C successfully in conjunction with corpus luteum in the treatment of threatened abortion. He suggests the use of vitamin C in the treatment of polymenorrhœa. Kramer, Harmon, and Brill⁹ have reported degeneration of both follicles and corpora lutea in scorbutic guinea-pig, as well as a failure to become pregnant or to deliver normal young. Ingier¹⁰ has shown in guinea-pigs that on scorbutic diets in early pregnancy, animals were born dead or prematurely. Bourne,¹¹ however, has reported that pregnant guinea-pigs remain normal on a scorbutic diet.

Biskind and Glick¹² have shown that the singularly high concentration of vitamin C in certain physiologically-related endocrine organs is striking. Of all animal tissues which they studied, the adrenal cortex, corpus luteum, and the anterior lobe and pars intermedia of the hypophysis are the richest sources; and of these, the

pars intermedia contains vitamin C in the greatest concentration. The correlation between vitamin C concentrations of functionally-related portions of the adrenal and hypophysis may be extended to the corpus luteum, which is physiologically related to the anterior lobe of the hypophysis, and contains vitamin C in approximately the same concentration. They showed that cows' corpus luteum contained 1.4 mgm. of ascorbic acid per gm. of tissue, when the organ was most fully developed; and that the value fell to 0.3 mgm. per gm. of tissue with regression. Biskind and Glick suggested that there may be a connection between the presence of vitamin C and the corpus luteum hormone progesterone. The corpus luteum, in pregnancy of the cow, has a concentration fifty per cent. higher than the mature corpus in the non-pregnant animal. Vitamin C^{13 14 15} seems to be unrelated to the female sex-hormone œstrin, but may be related to the hormone pregestosterone; as the vitamin¹⁶ content of the corpus luteum seems to be parallel to the pregestosterone content. Proper¹⁷ embryo implantation and continuance of gestation depends upon the presence of a corpus luteum, or even more exactly, on the progesterone it produces. When it is recalled that vitamin C deficiency produces degeneration of corpus lutea and failure of normal gestation in guinea-pigs, it would appear at least reasonable to suggest, that the vitamin is necessary for the normal production of the hormone, either by maintaining the integrity of the structures responsible for its formation, or more directly, by influencing the chemical reactions involved in the pregestosterone synthesis. Pillay¹⁸ measured the amount of vitamin C excreted in the urine of eleven women, through twenty-four menstrual cycles, and obtained some evidence in support of a theory, that there was decreased excretion of vitamin C at the time of ovulation. Bourne¹⁹ has suggested that vitamin C is associated non-specifically with the production of the corpus luteum hormone. Biskind and Glick used a special technique. They removed pieces of the corpus luteum of cows in different stages of function; cut sections of a certain thickness, and estimated the vitamin C content of the sections.

The knowledge that vitamin C has an effect in preserving the efficiency of the skeletal structures of the blood vessels, and also its relationship to the endocrine organs associated with menstrual function, would lead one to believe that vitamin C deficiency plays a part in the causation of the "nutritional anæmia" present amongst the women of industrial populations, not only in its effect on the hæmoglobin content per se, but also in its effect on the menstrual function, either by the production of an unhealthy condition of the walls of the blood vessels of the endometrium or by a derangement of the mechanics of the menstrual function through the effect of its deficiency on the formation of an essential hormone.

To test the truth of this assumption, a group of women who suffered from menorrhagia, with or without dysmenorrhœa, and who were of a similar social type to that of the Aberdeen sample, were given large doses of vitamin C (Redoxon tablets), and the results observed. Unmarried women were selected, as it was thought that they were less likely to be affected by extrinsic pathological factors. The sample numbered thirty-nine persons, and the ages ranged from fourteen to thirty-two, the average age being 21.6. As the sample was drawn from persons

in my practice, and who underwent the experiment voluntarily, objective tests of the menstrual function were not practicable, or do I know of any satisfactory method applicable to such a work as this. Observations were therefore limited to the duration of the periods and to the subjective clinical conditions associated. Weekly hæmoglobin tests were carried out by means of a Hall-Dare hæmoglobinometer. Comparisons were made between menstrual periods before and after the administration of the ascorbic acid.

Since it was not possible to carry out gynæcological examinations to include pathological conditions, it may be accepted that, as certain of the women may have had gynæcological conditions (pathological) responsible for their menorrhagia, they were not likely to be improved by the vitamin C treatment. The method adopted was to give each woman six thousand mgm. of vitamin C in Redoxon tablets, each of fifty mgm., the daily dose depending on the number of days usual in the cycle, care being taken that there was ample time to consume the whole test amount. Where the experiment was carried on for two months, a similar quantity was given during the second month. As it was considered that two hundred mgm. was the necessary daily quantity of vitamin C to completely saturate the body in the given time, and since the average duration of the cycle might be expected to be thirty days, the total dose was therefore six thousand mgm.

The aim in selecting the sample was to obtain ordinary women of the poorer class, who were suffering from menorrhagia and whose means were such that it might be expected that they were existing upon deficient diets. Many were anæmic and considered themselves run-down. They are a type met with constantly in general practice. During the experiment, one woman became pregnant, and in two other cases there was such irregularity in the menstrual cycle, that consideration of these two cases was not possible. In two other cases, their periods returned within a few days of the commencement of the treatment; the tablets were blamed, and they refused to continue. An unusual feature was, that for the first few days many of the women complained of severe headaches while taking the ascorbic acid, and which in one case was so bad that she was unable to continue. An attempt was made to establish a control group, who were given citric acid tablets, made to imitate the Redoxon ascorbic acid, but this was given up, and reliance placed on control by statistical methods devised for the experiment by Dr. Geary. The results are given in the following tables.

DISCUSSION.

Although scurvy is now relatively rare, it is evident that sub-clinical scurvy is relatively common. The clearest statement on the matter is that of Orr,²⁰ who, as a result of a study of diet in relation to income in Britain, proved that fifty per cent. of the population live on diets deficient in vitamin C and minerals. Foodstuffs containing vitamin C, with the exception of potatoes, are relatively expensive. It can therefore be easily understood why the sub-scorbutic condition is so prevalent.

In the account of the literature associated with this experiment, it is seen that vitamin C deficiency may play a part in producing nutritional anæmia: (a) by causing scurvy anæmia, (b) by causing menorrhagia, either by impairing the health

TABLE 1
MENORRHAGIA EXPERIMENT

Case No.	DURATION OF PERIOD IN HOURS						CLINICAL CONDITION AFTER TREATMENT					
	Before taking Ascorbic Acid		After taking Ascorbic Acid		Decrease		Menorrhagia		Dysmenorrhœa		Associated Symptoms	
1	...	72	...	54	...	18	...	2	...	2	...	2
2	...	90	...	80	...	10	...	2	...	2	...	2
3	...	96	...	108	...	12*	...	1	...	1	...	1
4	...	108	...	48	...	60	...	2	...	2	...	2
5	...	127	...	96	...	31	...	2	...	X	...	2
6	...	130	...	96	...	34	...	2	...	2	...	2
7	...	137	...	144	...	7*	...	2	...	2	...	2
8	...	120	...	132	...	12*	...	0	...	2	...	2
9	...	68	...	63	...	5	...	2	...	0	...	0
10	...	192	...	96	...	96	...	2	...	2	...	2
11	...	120	...	48	...	72	...	2	...	2	...	2
12	...	102	...	72	...	30	...	1	...	2	...	2
13	...	96	...	93	...	3	...	2	...	X	...	2
14	...	180	...	132	...	48	...	1	...	1	...	2
15	...	170	...	120	...	50	...	2	...	0	...	2
16	...	72	...	90	...	18*	...	0	...	2	...	2
17	...	132	...	120	...	12	...	2	...	2	...	2
18	...	120	...	96	...	24	...	2	...	2	...	2
19	...	95	...	96	...	1*	...	2	...	2	...	2
20	...	90	...	60	...	30	...	2	...	2	...	2
21	...	138	...	130	...	8	...	1	...	1	...	0
22	...	120	...	72	...	48	...	2	...	2	...	2
23	...	120	...	88	...	32	...	1	...	0	...	0
24	...	112	...	72	...	40	...	2	...	2	...	2
25	...	96	...	90	...	6	...	2	...	1	...	2
26	...	60	...	108	...	48*	...	2	...	2	...	2
27	...	168	...	90	...	78	...	1	...	2	...	0
28	...	96	...	96	...	0	...	0	...	0	...	0
29	...	114	...	120	...	6*	...	1	...	1	...	0
30	...	192	...	116	...	76	...	2	...	1	...	2
31	...	98	...	72	...	26	...	1	...	0	...	1
32	...	48	...	60	...	12*	...	0	...	X	...	0

X—Absence of symptoms before and after treatment.

0—No change in symptoms after treatment.

1—Improvement.

2—Completely normal condition.

*—Increase.

“Associated symptoms” are such symptoms as constipation, debility, listlessness, fatigue, loss of appetite, pains related to ovarian dysfunction, but not readily classified as dysmenorrhœa.

Total number of periods observed—110.

of the blood vessels of the endometrium or affecting the menstrual function in some unexplained way, probably associated with the formation of the hormone progesterone.

Anyone engaged in general practice in a poor area will be familiar with the type of woman of whom the sample was composed. In districts where there is much

TABLE 2
HÆMOGLOBIN FIGURES (GRAMMES PER 100 C.C.)

Case No.	Initial Finding	AFTER TAKING ASCORBIC ACID.				AFTER PERIOD			
		7th Day	14th Day	21st Day	Average Cols. (3)-(5)	7th Day	14th Day	21st Day	Average Cols. (7)-(9)
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
1	15.2	14.6	14.4	16.0	15.0	15.2	14.8	14.8	14.9
2	12.8	13.0	13.6	12.4	13.0	—	12.4	—	12.4
3	12.2	12.4	13.4	12.4	12.7	12.8	12.6	13.0	12.8
4	9.0	10.4	12.4	12.8	11.9	—	—	—	—
5	12.8	14.6	—	—	14.6	—	—	—	—
6	11.0	14.0	12.4	—	13.2	—	—	—	—
7	12.2	12.8	13.2	12.4	12.8	—	—	—	—
8	10.8	12.6	11.8	—	12.2	10.8	12.2	12.2	11.7
9	13.8	13.4	13.0	—	13.2	12.4	12.0	—	12.2
10	11.6	12.4	13.2	—	12.8	—	—	—	—
11	13.0	13.6	14.2	—	13.9	—	—	—	—
12	12.2	13.2	15.0	—	14.1	14.2	14.6	—	14.4
13	11.6	12.8	13.2	—	13.0	12.4	—	—	12.4
14	12.8	13.6	13.2	14.4	13.7	13.0	14.6	15.0	14.2
15	13.0	13.4	12.4	13.2	13.0	14.0	14.6	14.6	14.5
16	13.2	14.0	14.8	—	14.4	13.6	—	—	—
17	10.0	10.8	10.8	12.4	11.3	11.2	11.0	10.0	10.7
18	12.8	13.4	14.0	14.8	14.1	12.2	13.0	—	12.6
19	10.8	10.8	11.4	11.4	11.2	12.6	11.6	12.2	12.1
20	12.0	12.4	14.0	15.2	13.9	15.6	—	—	—
21	10.4	10.2	10.0	10.2	10.1	10.2	9.5	10.6	10.1
22	13.4	13.6	—	—	13.6	12.8	—	—	12.8
24	10.4	11.4	—	—	11.4	12.6	14.8	15.2	14.2
25	14.0	14.8	13.0	13.4	13.7	12.8	15.0	14.6	14.1
26	13.8	14.0	13.6	13.8	13.8	13.6	14.4	14.4	14.1
27	12.4	12.0	12.4	—	12.2	12.4	12.6	—	12.5
28	14.4	14.4	14.0	13.8	14.1	14.6	15.4	13.8	14.6
29	13.0	13.6	14.4	15.0	14.3	15.0	14.4	15.0	14.8
30	12.4	12.8	—	—	12.8	13.0	—	15.0	14.0
31	12.0	12.4	11.8	13.4	12.5	13.6	—	13.0	13.3
32	12.4	13.0	13.8	14.4	13.7	—	13.6	—	13.6

The sequence is that immediately following on the hæmoglobin test, known as the initial finding, the subject commences to take the ascorbic acid. The blood is again tested on the seventh, fourteenth, and twenty-first days after. Then follows a menstrual period, and again the blood is tested on the seventh, fourteenth, and twenty-first days after the period has ended.

TABLE 1A
Summary of Menorrhagia Experiment (derived from Table 1) as regards Duration
of Period

Cases in which Duration of Menstruation Prior to Treatment was—				Number of Cases	Average Duration of Period in Hours			Average Decrease (–) or Increase (+)	
					Before Treatment		After Treatment		
I.	127 hours or more	...	10	...	157	...	114	...	– 43
II.	98 hours to 120 hours	...	10	...	113	...	82	...	– 31
III.	96 hours or less	...	12	...	82	...	84	...	+ 2
All cases		...	32	...	115	...	92	...	– 23

TABLE 1B
Summary of Menorrhagia Experiment (derived from Table 1) as regards Clinical
Conditions after Treatment

Cases in which After Treatment there was—					NUMBER OF CASES				
					Menorrhagia		Dysmenorrhœa		Associated Symptoms
(a)	Completely normal condition	20	...	18	...	23
(b)	Improvement but not normal condition	8	...	6	...	2
(c)	No change in symptoms	4	...	5	...	7
(d)	Absence of symptoms (before and after treatment)	—	...	3	...	—
All cases					...	32	...	32	...

TABLE 2A
Summary of Hæmoglobin Experiment (derived from Table 2)

Initial Hæmoglobin Figures (inclusive)		Number of Cases		Average Hæmoglobin Figures Per Case Before After			Average Increase		
9.0 to 12.0	...	11	...	10.9	...	12.1	...	1.2	
12.2 to 12.8	...	10	...	12.4	...	13.4	...	1.0	
13.0 to 15.2	...	10	...	13.8	...	13.9	...	0.1	
All cases		...	31	...	12.3	...	13.1	...	0.8

female employment, they are particularly common. Such persons are usually pale, thin, and listless. They are easily tired, with poor appetites, are often constipated, and live in constant dread of their monthly ordeal. In the course of the experiment, it was a particular pleasure to observe the improvement, often dramatic, which the ascorbic acid made in their condition. In several of the cases, this was the first period for years in which they had not been forced to leave work and go to bed. Constipation, headaches, and constant perineal pain cleared up in almost every case where such conditions were present. Although it was not possible to transform such clinical observations into figures, these features, together with an improvement in well-being and diminution in blood-loss, were the most noteworthy results of the experiment.

SUMMARY.

- (1) An experiment has been carried out on thirty-two unmarried females of the

industrial class, all of whom were suffering from menorrhagia, to demonstrate the relationship between vitamin C deficiency and nutritional anæmia due to menorrhagia.

(2) After a test dose of ascorbic acid (Redoxon) sufficient to produce saturation, of the thirty-two cases, twenty were restored to a clinically completely normal condition, eight were improved, but not normal, and four had no change in symptoms.

(3) There was a diminution in the duration of the menstrual periods and an increase in hæmoglobin.

(4) Improvement was greatest in the worst cases.

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STATISTICAL COMMENT

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TABLE 1.—The fact that in all but eight cases out of thirty-two a reduction in the duration of period following the use of ascorbic acid establishes a *prima facie* case of significant relationship. On the average, the reduction amounted to twenty-three